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## Behavioral Circadian Regularity at Age 1-Month Predicts Anxiety Levels During School-Age Years

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### Abstract

Daily lifestyle regularity is measured using the Social Rhythm Metric (SRM). We developed a Baby SRM, with 59 babies followed for ~13 years. Baby SRM score at age 1-month significantly predicted the child's school (K-9, 5 timepoints) anxiety level (more regular = less anxious), and may be mediated through sociability and directed-attention pathways.

### Keywords

Circadian rhythms; development; anxiety; longitudinal

## 1. Introduction

Human circadian rhythms research has long been dominated by concern regarding how circadian rhythms might lead to or exacerbate psychiatric disorders such as depressive, bipolar, and anxiety disorders, when they are running at an inappropriate timing or in an irregular fashion (Wehr and Goodwin, 1983). Much of this work has been concerned with *physiological* circadian rhythms in body temperature, cortisol and melatonin. However, even when *behavioral* circadian rhythms are considered, as measured by questionnaires and diaries, patients may have rhythms that are very different to healthy controls in their timing (Wood et al., 2009) or regularity (Shear et al., 1994), or both.

A patient's level of daily lifestyle regularity for a particular week can be measured using a diary instrument, the Social Rhythm Metric (SRM) which yields a numerical score between 0 (least regular) and 7 (most regular) (Monk et al., 1990). In healthy adults the SRM metric shows an approximately Gaussian distribution with a mean at about 3.4 and a standard deviation of about 0.8 (Monk et al., 1994). High SRM scores have been shown to relate to better sleep quality and to successful aging (Monk et al., 1992; Monk et al., 2003; Carney et

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al., 2006), and to be protective against bereavement-related depression in widow(er)s (Prigerson et al., 1996).

In adult psychiatric illness, low SRM scores have been observed in both depressed inpatients (Szuba et al., 1992) and outpatients with anxiety disorders (Shear et al., 1994). Moreover, therapies designed to enforce greater regularity in a person's daily routine (thus increasing the SRM score) have been shown to help bipolar patients (Frank et al., 2005). Thus, underlying differences in the circadian timekeeping system driving the habitual timing of daily events may be associated with varying levels of psychopathology.

Because parents are adults with well-developed daily behavior patterns, an infant's level of circadian regularity will determine the nature of his or her interaction with them, and may thus affect early attachment relationships and the development of self-regulatory social skills in infancy. Greater infant sociability is positively related to maternal contact and responsiveness at ages 1, 3, and 9 months (Fish et al., 1981), and secure infant attachment predicts lower levels of child and adolescent anxiety disorders (Warren, et al., 1997). Stronger and more regular circadian rhythms in the infant may increase the predictability of infant demands, leading to enhanced parental perception of need cues (Crockenberg and Leerkes, 2000) and increase parental confidence (Leerkes and Crockenberg, 2002) which might further strengthen care-taking routines. Infant social behaviors, such as smiling, are in part self-regulatory, and aid in coping with both physical and social stimulation (Sroufe and Waters, 1976). Mothers and fathers, whose infants exhibited significant increases in regulation and predictability from age 3 to 9 months, displayed increased sensitivity during play and greater caretaking involvement (Feldman et al., 1997). Thus, stronger and more regular circadian rhythms in the infant may enhance early parent-infant relationships and further improve infant regulatory capacity.

Temperamental rhythmicity as described by Chess and Thomas (1996) is quite similar to the current construct of Baby SRM (see below) and refers to the predictability or unpredictability in time of the sleep-wake cycle, hunger, feeding, and elimination. Children low in temperamental rhythmicity are likely to be classified as having a difficult or dysregulated temperament, and difficult or dysregulated temperament has been reliably associated with greater risk for psychopathology, including symptoms of anxiety (Rende 1993; Warren and Simmens 2005).

The capacity of directed-attention is a self-regulatory skill related both to cognition and emotion (Eisenberg et al., 2000). Self-regulatory and self-directed capacities are important to the development of adaptive functioning (Rothbart et al., 2000). The enhanced parent-infant and caregiver-infant relationships resulting from consolidation of an infant's alert time into daylight hours, is likely to support and strengthen such self-regulation, allowing more internal resources to be devoted to environmental exploration (Ranson and Urchuk, 2008). Moreover, attentional processes may help to modulate emotional arousal (Derryberry and Reed 1996; Rothbart et al., 2000). and to manage overt behavior when emotion is not adequately regulated by other means (Eisenberg et al., 2000). Children high in effortful control exhibit lower levels of internalizing symptoms, like anxiety (Lengua et al., 2008). Thus, an infant's ability to direct attention may represent greater self-regulation, and is perhaps associated with stronger and more regular circadian rhythms.

Recently, major progress has been made in the field of circadian rhythms, leading to a much better understanding of the underlying mechanisms. In particular, it now appears there are genetic polymorphisms which can determine the individual's preferred circadian phase or chronotype (Jones et al., 2007). It is also likely (though yet to be demonstrated) that there may be a genetic basis to the extent to which an individual's behavior patterns are influenced

by the circadian timekeeping system, and thus the extent to which he/she is habitually regular or irregular in the timing of his/her daily events. This led to the observation (confirmed anecdotally by parents with multiple children) that *from birth* some babies adapt almost immediately to a 24h routine and thus sleep through the night, while others (even within the same family) may take considerably longer. It was thus of interest to us what the level of an individual's 24h rhythmicity in behavior might be, even as early as one month after birth. We thus constructed a baby analogue to the adult SRM. We then related baby SRM score to the child's depression and anxiety symptoms more than a decade later, while the child was at school.

## 2. Methods

In order to measure lifestyle regularity in babies, we used a diary instrument (referred to here as the Baby SRM) completed by parents, by which very young babies' routines could be measured a week at a time. In 1990 and 1991, as an add-on to a much larger study of new parents co-directed by M.J.E., the Baby SRM diary was completed by 59 couples for 2 consecutive weeks when their infant was one month old. The diary was a structured instrument which accepted sleep as the baseline behavior and required the parent to write down the starting time for each of four other major daily events in the infant's life, listed as feeding, playing, diaper changing and receiving comfort (other variables regarding the day's activities were also asked but will not be discussed here). There were 30 baby girls and 29 baby boys; all were born after at least 28 weeks of gestation; all but two after 37 weeks of gestation.

Only recently, did one of us (A.M.S.) develop an algorithm by which a numerical Baby SRM score could be derived. Baby SRM score was determined by an algorithm which cast the four specified events in the infant's daily life (feeding, playing, diaper changing and receiving comfort) into twelve 2h bins covering the 24h day, then summing over a week. The metric (see appendix) related to how "spikey" versus flat the resulting time-of-day curve was, averaging over the four events. Thus, a flat curve would indicate events spread evenly around the clock, a spikey curve that particular times of day predominated. Thus, the more spikey the curve, the higher (more regular) the Baby SRM score. Parallel to the adult SRM, the Baby SRM score ranged from 0 (least regular) to 7 (most regular). The two scores from a fortnight were averaged. This work was done at the University of Pittsburgh blind to the knowledge that follow-up data had ever been collected. It was only after individual Baby SRM scores had been calculated, that the Pittsburgh team became aware that follow-up data from these children had been collected by their colleagues at the University of Wisconsin at Madison. In a similar vein, all of the follow-up data to be described was collected totally blind to the Baby SRM scores (which at the time had not yet been calculated).

Because of the known link between circadian function and mood/anxiety disorders, we here focused on children's depression and anxiety symptom levels at school-age. We correlated each infant's SRM score at age 1-month with the average (mother-rated) level of depression and anxiety symptoms in that child. Mental health symptoms in the school-age children were assessed using mother reports from the MacArthur Health and Behavior Questionnaire [HBQ; (Boyce et al., 2002; Essex et al., 2002)]. Mothers rated 7 items (ages 6 and 7 years), 13 items (age 9 years) and 16 items (ages 11 and 13 years) measuring Depression (e.g., "Cries a lot"); 12 items (ages 6 and 7 years), 10 items (age 9 years), 11 items (age 11 years), and 12 items (age 13 years) measuring Anxiety (e.g., "Worries about things in the future"). Mothers rated each item on a 3-point scale ranging from 0 (*never or not true*) to 2 (*often or very true*). Higher scores represented higher symptom levels. Alpha coefficients for mothers' ratings of Depression ranged from 0.64 to 0.80, and for ratings of Anxiety from 0.76 to 0.79, across all time periods.

Follow-up data were also available related to the children's sociability. At ages 4 and 12 months mothers and fathers completed the Infant Behavior Questionnaire [IBQ; (Rothbart 1981; 1986)], a structured parental report assessing motor activity, vocal activity, and integrated emotional expression. Three individual items measuring smiling and cuddling behavior were chosen from this measure to comprise a measure of infant sociability (e.g., "In the past two weeks how often did your baby not like to be cuddled or touched?", "In the past two weeks how often did your baby smile and act responsive or affectionate?"). Items were rated by the mother and father using a 7-point scale ranging from 1 (*never*) to 7 (*always*). These ratings were combined across time for each parent using unrotated principal components analysis to yield a composite infancy cuddle-smile score. Higher scores indicated greater cuddling and smiling behavior. Because mothers' and fathers' cuddle-smile score were correlated ( $r = 0.45, p = 0.001$ ) the average of these composite scores was used in all analyses. Although not a direct measure, mothers' and fathers' ratings of their infant's cuddling and smiling behavior serve as a proxy of the quality of the parent-child relationship as children with poor quality relationships exhibit these behaviors less frequently, particularly later in infancy. Greater smiling and smiling combined with vocalizing distinguish securely attached children from insecurely attached children at both 18 and 24 months of age (Waters et al., 1979). Infant smiling at age 6 months is positively correlated with anticipatory smiling during episodes of joint attention at 8 and 10 months, and with greater social expressivity at age 30 months (Parlade et al., 2009). Anticipatory smiling is indicative of intentional, voluntary communication (Jones and Hong, 2001).

Regarding attention skills, a measure of directed-attention was obtained from videotaped observations of a two-hour home visit when children were 4½ years of age. Ratings were made by a child tester and camera operator who observed the child during a series of emotion-eliciting tasks from the Preschool Laboratory Temperament Assessment Battery (Goldsmith et al., 1993) and mother-child interaction tasks (Snack Time, Structured Block-Building, Free Play) from the Parent-Child Early Relational Assessment (Clark, 1999). After the visit, the child tester and camera operator reviewed the videotape and independently rated each child on items characterizing emotional and behavioral tendencies. Items were rated on a 5-point scale ranging from 1 (Complete lack of, or minimal evidence for, the quality being rated) to 5 (*An intense, consistent, and/or extreme reaction*). Observers' ratings were averaged to produce scale scores, and all kappa values exceeded 0.76. For the present study, the average of two scales reflecting Interest and Initiative was used to represent the construct of directed-attention.

It should be noted that all of these measures were obtained in non-overlapping time periods (Baby SRM at 1month, cuddle-smile at 4 and 12mos, directed-attention at 4.5y, and depression and anxiety at 6y – 13y).

Descriptive statistics were compiled for predictor and outcome variables. Separate one way analyses of variance (ANOVA) were conducted to check for differences in variable between boys and girls (no significant differences were observed). Zero-order Pearson correlations among predictor and outcome variables were calculated. The two proposed pathways were tested using a series of regression models and Sobel's tests for mediation. All statistical indices for skewness and kurtosis were within the acceptable range and it was concluded that all variables conformed to a relatively normal distribution.

### 3. Results

Using the Baby SRM scoring algorithm (see Appendix), the sample of 59 babies was found to have a mean SRM score of 3.03 with a standard deviation of 0.54. The distribution of scores was approximately Gaussian, with a range from 2.2 to 4.6. Baby SRM score appeared

to relate to the 24h behavioral regularity of the infant. High scoring babies, for example, were less likely to need a feed during the night than were low scoring babies. Pearson correlation coefficients are reported in Table 1.

Because the time-to-time correlations of depression and anxiety symptom levels were quite high (range:  $r=0.34$  to  $0.84$  for depression,  $r=0.46$  to  $0.71$  for anxiety), averaging across time provided a more reliable estimate of overall symptom levels across the child's early school-age years. Baby SRM score was significantly correlated with school-age anxiety symptoms, with higher (more regular) SRM score associated with lower overall levels of anxiety symptoms. The sex of the child had no effect upon this association. A similar pattern was observed across the five separate time points (age 6, 7, 9, 11, and 13 years,  $r = -0.35, -0.37, -0.24, -0.26,$  and  $-0.30,$  respectively). There was no significant correlation of Baby SRM with child depression. When co-morbidity was taken into account (by including depression in a multiple regression analysis of the effect of Baby SRM on childhood anxiety levels), the effect of anxiety remained significant.

Regarding sociability, cuddle-smile (at 4 and 12 mos.) was correlated both with Baby SRM score at age 1-month, indicating greater sociability associated with greater regularity; and with school-age anxiety indicating greater sociability associated with lower anxiety. Directed-attention at 4.5y was *not* correlated with infant cuddle-smile. However, directed-attention was correlated both with Baby SRM score (indicating greater directed-attention associated with greater regularity), and with school-age anxiety (indicating greater directed-attention associated with lower anxiety). Again, it should be noted that the time-points did not overlap.

The application of a series of regression models and Sobel's tests for mediation revealed the following: The first path tested was that of SRM to Cuddle-Smile to Anxiety. The first step entered only SRM as a predictor of Anxiety. SRM significantly predicted later Anxiety ( $B = -0.17, SE = 0.06, p = 0.007$ ). In the second step both SRM and Cuddle-Smile were entered into the model. Cuddle-Smile significantly predicted later Anxiety ( $B = -0.09, SE = 0.03, p = 0.034$ ) and the initial effects of SRM were reduced ( $B = -0.11, SE = 0.07, p = 0.094$ ), suggesting mediation. We then conducted Sobel's test which revealed that the mediation of SRM by Cuddle-Smile was marginally significant ( $p = 0.06$ ).

The second path tested was that of SRM to Directed-Attention to Anxiety. The first step entered only SRM which significantly predicted anxiety ( $B = -0.10, SE = 0.04, p = 0.037$ ). The second step entered SRM, Directed-Attention, and Depression into the model. Directed-Attention significantly predicted later Anxiety ( $B = -0.12, SE = 0.04, p = 0.010$ ) and the initial effects of SRM were reduced ( $B = -0.05, SE = 0.05, p = 0.289$ ), but only when co-occurring depressive symptoms were controlled. We then conducted Sobel's test which indicated a significant mediation of SRM by Directed-Attention ( $p = 0.04$ ) when co-occurring depression was controlled. Thus, Cuddle-Smile mediated the effects of SRM on Anxiety with or without co-occurring depression; and Directed-Attention mediated the effects of SRM on pure Anxiety, when co-occurring depression was statistically controlled.

#### 4. Discussion

When one remembers that the sampling periods for the different variables were totally non-overlapping, the magnitude of these effects is particularly striking. Correlations with Baby SRM score ranged from  $0.35$  to  $0.47$  (Table 1) suggesting that between 12% and 22% of the variance was explained. Thus, daily behavioral regularity in the life of a 1-month old infant appears to be predictive of anxiety levels more than a decade later, during the school-age years. This relation appears to be mediated through sociability and directed-attention



pathways, even though measures of sociability and directed-attention were obtained before the child had even started school, and were not themselves inter-correlated. This bespeaks the potential importance of the circadian system and its development in the life of the child.

The lack of any effect in depression was not unexpected because no simple relationship between SRM and depression had emerged in our sub-clinical adult samples (Monk et al., 1991). Moreover, our earlier work has also shown that the lower SRM scores of anxiety disordered patients (compared to normal controls) were not accounted for by the presence of comorbid mood disorders (Shear et al., 1994). However, the present finding may also reflect the developmental period of childhood when anxiety symptoms are more prevalent and before the increase in depression during adolescence (Kessler et al., 2001; Costello et al., 2005).

Regarding the sociability pathway between Baby SRM and school-age anxiety, we note that supporting infants' self-regulatory capacities is the quality of relationships with caregivers. Greater regularity to daily activities may increase the predictability of infant demands leading to enhanced parental perception of need cues (Crockenberg and Leerkes, 2000) and increased parental confidence (Leerkes and Crockenberg, 2002) which further strengthens care-taking routines. Thus, greater regularity to daily activities may enhance early parent-infant relationships, improve infant regulatory capacity and promote environmental exploration as internal resources are available (Ranson and Urichuk, 2008). Such exploration encourages later cognitive development as the infant encounters new challenges.

In conclusion, we propose a 2-pathway model whereby daily regularity at age 1-month, as measured by the Baby SRM, was related to school-age anxiety through individual differences both in sociability and in directed-attention, even though sociability and directed-attention were not themselves inter-correlated. This relationship may, or may not, reflect a shared genetic foundation for both circadian and mental health variables (e.g. Wood et al., 2009). Further work is needed to explore the genetic underpinnings of the present sample.

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## Appendix

The algorithm for deriving the Baby SRM score was as follows: Four activities were considered: feeding, being comforted, play, and diaper change. For the purpose of creating distributions, a binning method was used to divide 24 hours into twelve 2-hour bins (0:00 – 1:59, 2:00 – 3:59, 4:00– 5:59, etc.). If the timing of an activity occurred (started) within a given bin, the count was then incremented for that bin. This created a distribution for the completions of an individual activity, with spikes in the distribution indicating the time of a more regular occurrence. The following process was done individually for each of the 4 activities. The total number of completions of a given activity over 7 days was tabulated for variable  $c$ . Then, the quantity  $x$  (the number of bins that have at least one occurrence of an activity) was calculated. In order to determine the cut-off level for regularity, we first counted the number of completions ( $c$ ) each bin ( $x$ ) would have if the completions were distributed evenly across  $x$  bins ( $\text{int}[c/x]$ ). The integer  $z$  was representative of how many bins

had hits greater than or equal to  $\text{int}[c/x]$ . If  $\text{int}[c/x]$  was less than 3, the cut-off for 'regularity' was automatically set to 3. The next step was to calculate the proportion of bins with a number of completions above the set level ( $z/x$ ). The proportions were then summed from each activity and divided by the number of activities that had 3 or more completions ( $a$ ). This averaged proportion was then multiplied by 7 to get the SRM score on a scale from 0 to 7. Thus, Baby SRM score =  $7 \sum [(z/x)/a]$ .

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**TABLE 1**

Results of correlational analysis using Pearson r statistic (n=59).

	Mean (SD)	Age 1 month Baby SRM	Age 4 and 12 months Cuddle-Smile	Age 4 1/2 years Directed Attention	Age 6,7,9,11, and 13 years Anxiety
Age 1 month Baby SRM	3.03 (0.54)	---			
Age 4 and 12 months Cuddle-Smile	-0.02 (0.87)	0.35**	---		
Age 4 1/2 years Directed Attention	3.75 (0.54)	0.47**	0.13	---	
Age 6,7,9,11, and 13 years Anxiety	0.51 (0.25)	-0.35**	-0.30*	-0.40**	---
Age 6,7,9,11, and 13 years Depression	0.26 (0.20)	-0.22	-0.26	-0.12	0.78**

\*\*  $p \leq 0.01$

\*  $p \leq 0.05$